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Oculomotor reflexes as a test of visual dysfunctions in cognitively impaired observers

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Introduction

The project aims to develop a battery of tests to diagnose visual dysfunctions in cognitively impaired observers based on their oculomotor reflexes. The oculomotor reflexes provide a simple and robust method to study vision in passive/immature/impaired observers. For example, oculomotor reflexes are widely used to study vision in infants and in marketing research. The proposed method is versatile, applies to a wide range of visual mechanisms, and can provide both qualitative (yes/no) and quantitative (degree) estimates of the visual loss. The project embodies a full research and development cycle, from establishing the most effective stimuli for various kinds of visual dysfunctions to the design of a computerized testing kit suitable for use by non-specialists. After a short training course, the kit could be used at army bases and local hospitals to make a quick initial diagnosis.

Body

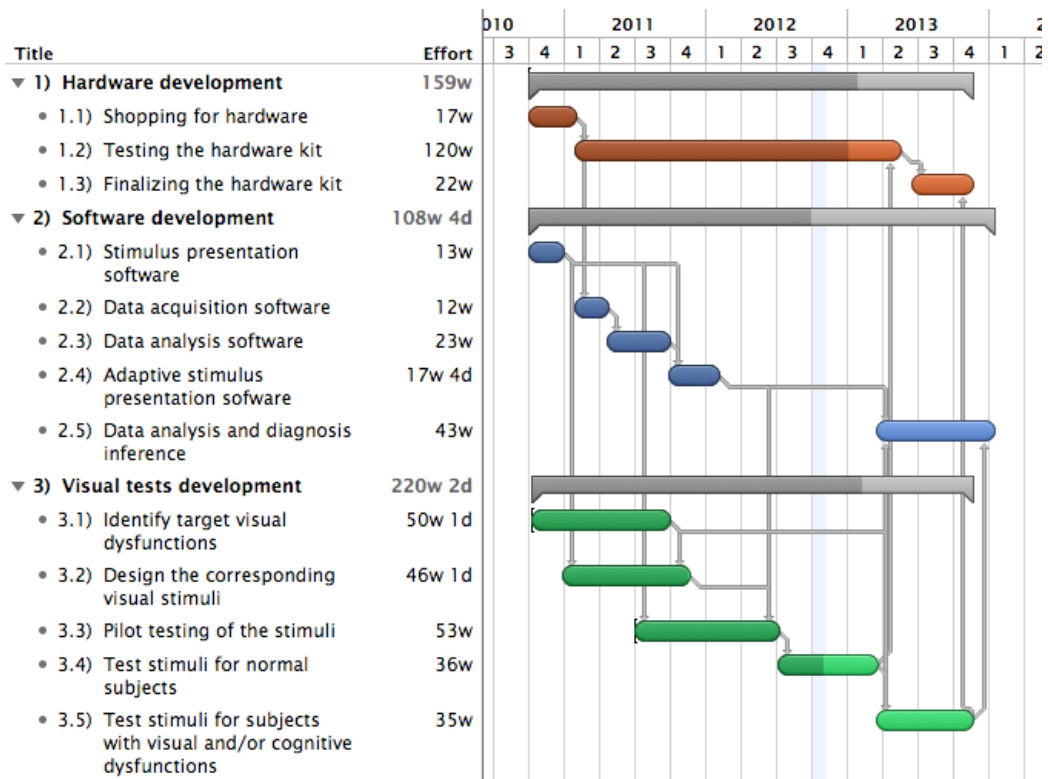


Figure 1: Gantt chart for the project.

As specified in the Statement of Work, the main goal of the second 12-months period of the project was to make the tools developed in the first aim available to non-specialists. To this end, a computerized testing kit based on an automatic eye-event registration algorithm was developed. The kit is used to present visual stimuli, collect eye-position and pupil-size data and search the data for relevant ocular reflexes evoked in a real-time automated regime. Based on the analysis, an adaptive algorithm chooses/adjusts the

test stimuli for the next round of stimulation until a certain reliability level is achieved and the battery of tests is exhausted. At the moment the test results are presented as percent correct scores. Once the full statistics on normal observers and observers with visual dysfunctions is collected the results will be presented in the form of probability scores for different kinds of visual dysfunctions.

Figure 1 shows a Gantt chart indicating project tasks and their current state of completion. Overall, all the current goals were met: the hardware kit was augmented for real-time data exchange between the video-presentation and data-collection laptops, a software counterpart for the data exchange was developed and tested, a large portion of the pilot stimuli were modified to their final form, algorithms for eye-event registration were improved and implemented in C++ within the same software package as the stimulus generation and data exchange. These tasks are described in detail in the following sections.

Hardware development



Figure 2: The complete hardware kit. The data-collection laptop is on the left, the video-presentation and data analysis laptop is on the right. The eye-tracker is in the center, its electronics (MiniLab) is in the back, the head-mounted eye cameras and IR mirror attached to a safety-google frame are in the front. The Keyspan serial-USB adapter connecting the eye-tracker to the data-analysis laptop can be seen in the center.

The hardware kit was completed in the first quarter. A photograph of the full kit (the head-mounted version) is shown in Figure 2. To ensure

maximum performance two computers (laptops) are used. One computer is dedicated to controlling the eye-tracker. Stimulus generation, presentation, data collection, and data analysis are carried out by another computer. The two computers communicate via serial connection. Eye images are sampled at 120 Hz by the ISCAN Inc. eye-tracker. 120 Hz was proven to be an adequate sampling frequency for our purposes. Video components of the eye-tracker include miniature eye- and scene-cameras, infrared (IR) illuminator LED, and an IR mirror all mounted on a safety-goggles frame positioned on a subject's head. The electronic components (MiniLab) include hardware-implemented algorithms for segmenting the pupil image from the eye image and calculating the pupil's position and size. MiniLab also includes hardware for the serial data output. The eye-tracker is controlled from the laptop shown on the left. ISCAN software installed on the laptop provides an intuitive graphical user interface (GUI) allowing to control the eye-tracker in a simple fashion. In particular, it is used to optimize the camera settings for various lighting conditions and, if required, for glasses or contact-lenses worn by the subject. The laptop shown on the right is used for visual stimulation and online analysis of the eye-tracking data. Visual stimuli are presented either on the laptop screen or on a dedicated monitor (not shown). The eye-tracking data is received in real-time regime from the MiniLab electronics via a 6 ft. serial cable. The data is received on a USB port of the laptop via a Keyspan serial-USB adapter (model USA-19HS).

The head-mounted version of the eye-tracker can be mounted on a baseball cap if the safety-goggles frame is not tolerated by the subject. If neither version of the head-mounted device can be safely worn by the subject the remote (desktop mounted) eye-tracker with automatic head tracking can be used. The remote eye-tracker will also be used for detecting dysfunctions in binocular convergence for all subjects, because it allows to track both eyes simultaneously.

The hardware kit was tested in both the PI's laboratory and in field conditions. In the latter case the kit was taken to the Brown University, where a subject with recent TBI-related visual dysfunctions was tested. The kit weighed about 20 pounds and was carried in a medium-sized backpack. It took less than 10 minutes to assemble the kit and to get it ready for the test.

Visual tests development

In the third quarter the pilot stimuli developed and tested during the first year were improved to produce more robust eye events suitable for automated

Reflex	Stimulus	Functions
Visual Nystagmus	luminance grating equiluminant grating contrast gratings at 3 spatial scales semi-coherently drifting dots	low-level motion color vision visual acuity high-level motion
Orienting Reflex	contour / texture boundary odd image (animal among males) seminude female vs. 'boring' male	low-level object processing mid-level object processing high-level object processing
Pupillary reflex	mild curse in a random word stream odd word within a sentence	mid-level reading high-level reading

Table 1: Oculomotor reflexes, the stimuli used to evoke the reflexes, and the corresponding tested visual functions.

detection. The ocular reflexes, the stimuli used to evoke these reflexes, and the corresponding tested visual functions are presented in Table 1.

We developed a new stimulus for visual nystagmus to test visual motion processing in the presence of incoherent motion noise. The drifting equiluminant color grating stimulus used for testing color deficiencies was redesigned to make the evoked visual nystagmus much more robust. Because the absolute gaze is not measured in our paradigm (this would require a gaze calibration, involving significant cooperation of the subject) the orienting reflex has to be measured with respect to an undefined gaze position at the time of the stimulus onset. To attract the gaze to the center of the screen a disk contrast-reversing for 500 msec is now presented at the center of the screen 1000 msec before the stimulus onset. In addition, the odd-ball image and contour/boundary stimuli used to evoke the orienting reflex were simplified to make the evoked eye movements less dependent on the gaze position at the time of the stimulus onset. To this end, the odd image or the contour/boundary was positioned in one of the 4 quadrants on the screen (compared to 8 such positions used in pilot stimuli). The test was considered passed if the subject's gaze stayed in the 'interesting' quadrant significantly longer than in the remaining quadrants. The odd-word stimulus originally designed to test the ability to read and comprehend isolated words was extended to include complete sentences, where the ability to understand the logical structure of a written text is also tested.

Software development

The four eye-event filters (blinks, saccades, nystagmus, and pupillary reflex) prototyped in MATLAB in the course of the previous year were implemented in C++. This allowed us to increase the filters speed and to unite stimulus generation and data analysis into a feedback loop within the same application running on the data-analysis laptop. The filters are based on measuring and thresholding eye-movement velocities and pupil area changes. From the start the filters were designed to be used with real-time data: they are fast and do not require large amounts of data. Less than a second of data is sufficient to detect saccades and pupillary reflex, and several seconds of data – to detect visual nystagmus which, typically, lasts for 3 – 5 seconds at a time. In the third quarter we thoroughly redesigned the nystagmus and pupil dilation filters to make their output more robust to subjective variations. To this end we developed a new algorithm, where the eye-tracking data is analyzed at different time scales and then the resulting filter outputs are integrated across the scales. We also completely redesigned the filter used to measure the orienting reflex (eye-movement and the following viewing of an interesting object). Instead of relying on the direction of the first saccade we used a different approach based on measuring how long the subject’s gaze stayed within the area of interest compared to the rest of the scene. This measure proved to be more robust to the effect of the (somewhat unpredictable) gaze position at the beginning of the trial.

Figure 3 illustrates the new filters performance. Raw eye-tracking data (a single trial in each case) are shown by the black symbols, the outputs of the corresponding filters are marked in red. Panel *a* illustrates a filter response to a significantly longer viewing of an odd (animal face) image shown in the bottom-right quadrant. Panel *b* illustrates a similar paradigm, where a semi-nude female image shown in the left half of the screen was viewed longer than a ‘boring’ male image in the right half. The filter response, again, indicates a significantly longer viewing of the ‘interesting’ image. Panel *c* illustrates a robust visual nystagmus arising in response to the stimulus where a coherent drift of some dots is masked by incoherent random movements of the remaining dots. Panel *d* illustrates a pupillary dilation in response to a mild curse word suddenly appearing within a sequence of ‘ordinary’ words presented on the screen.

Currently we are working on tweaking the visual stimuli and the respective filters to make the filter performance maximally independent of subjective variations in the eye-tracking data. This is most crucial while detecting the pupillary response to a surprising stimulus (e.g., a curse word), where the latency, amplitude, and duration of the pupil dilation were found to vary

significantly from trial to trial and also among subjects.

Testing

Once the Northeastern University IRB and MEDCOM USAMRMC approvals for work with human subjects were renewed in October 2011 we collected and analyzed data for twenty five normal observers and two observers with possible visual dysfunctions. Fifty more observers will be tested in the fourth quarter. The large number of observers is necessary to accumulate enough statistics to estimate the distribution of test scores (percent correct) among normal observers. This distribution will be used to convert the test scores to the probability of visual dysfunctions.

Northeastern University undergraduate students of both sexes 18 - 25 years of age with normal or corrected vision were recruited as normal subjects. The subjects were inexperienced observers naive to the purpose of the test. The only instructions received from the experimenter were to attend to the screen. The subjects and experimental conditions are meant to simulate testing cognitively impaired soldiers. We also carried out pilot tests of two subjects with recent history of visual dysfunctions. Subject S1 (a female, 37 years old) had a severe traumatic brain injury 8 months prior to the test. As a result, her control of eye movements was initially disrupted to the extent that for several months she could not read at all, could not do her work or travel. At the time of the test she described her visual functions as almost normal. Superficially, her eye movements also appeared normal. Subject S2 (a male, 70 years old) had a foveal retinal detachment in both eyes. A year prior to the test he was operated. The first operation was unsuccessful in the right eye, but after the second operation he reported his vision to be mostly restored in both eyes.

Experimental sessions lasted 6 minutes during which 80 visual stimuli were shown. Subjects were viewing stimuli on a 21" LCD monitor from a distance of 60 - 80 cm. The head-mounted version of the eye-tracker was used for all subjects, pupil (left eye) position on the camera's CCD was sampled at 120 Hz. The data were collected and analyzed by the developed software filters in real time and then saved on the hard drive of the data-analysis laptop. A fragment of the data and the accompanying automatic eye-event segmentation for one subject are shown in Figure 3. Compared to normal subjects, S1 showed lower scores in the odd-word experiment. This suggests that S1's reading speed was not restored to its normal rate. Subject S2 showed no equiluminant (color-defined) nystagmus and very low scores for contrast-defined nystagmus. This indicates that S2's foveal vision

was relatively poor, lacking in color sensitivity and acuity. Although at the current stage of the project it is too early to draw definite conclusions about the effectiveness of our approach, these pilot tests make us optimistic.

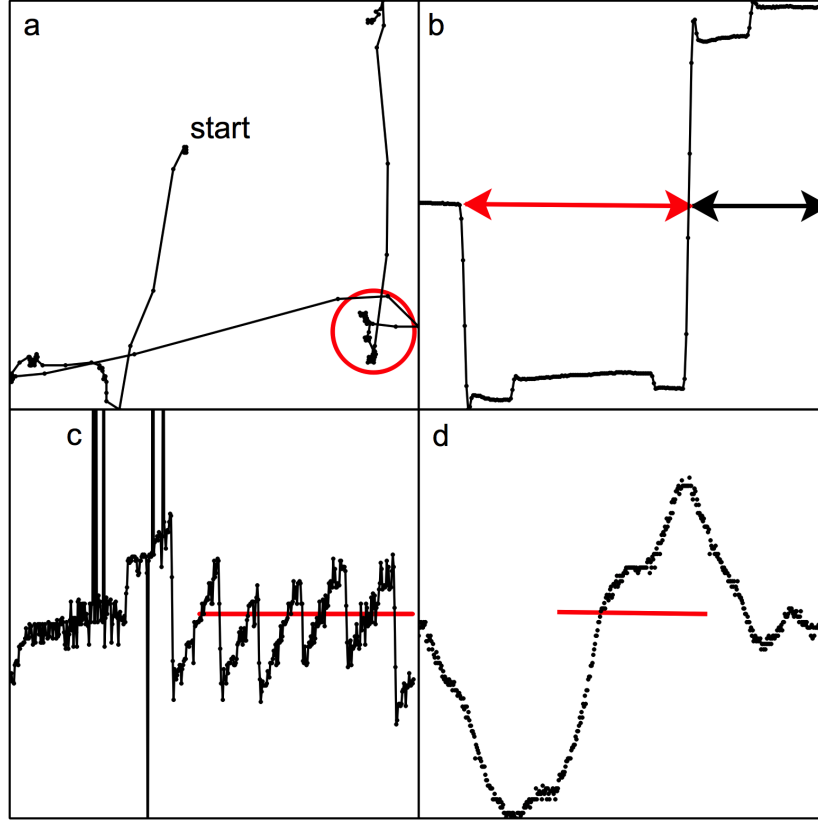


Figure 3: Eye tracking data and the corresponding filter outputs. Time from the stimulus onset is plotted along the x-axis in panels b – d. (a) An animal face was shown in the bottom-right quadrant, 3 human male faces were shown in the remaining quadrants. Gaze point readings (x and y coordinates on the camera's CCD) are marked by the black dots. Only 3 images were explored by the subject's gaze. The red circle indicates a significantly longer viewing of the bottom-right image detected by the filter. (b) a semi-nude Marilyn Monroe image was shown in the left half of the screen, a male figure in a suit was shown in the right half. Gaze horizontal position is plotted along the y-axis. A significantly longer viewing of the left image detected by the filter is indicated by the red arrow. (c) For the first quarter of the trial randomly placed dots were moving in a 'random walk' fashion, afterwards 25% of the dots were also drifting to the right. Gaze horizontal position is plotted along the y-axis. The red bar indicates a visual nystagmus event detected by the filter. (d) A mild curse word was displayed on a white background at the beginning of the trial. Pupil area is plotted along the y-axis. The red bar indicates pupil dilation detected by the filter. The pupil contraction at the beginning of the trial resulted from the response to the white background.

Key Research Accomplishments

- The hardware kit was finalized, its components and settings were tested and optimized.
- Real-time data exchange between the eye-tracker and the data-analysis computer was implemented and tested.
- Eye-event filters were redesigned to be less sensitive to individual variation in ocular reflexes. The filters were implemented in C++ and incorporated into the software running on the visual stimulation and data analysis laptop. The real-time processing of the data will be used to make the testing adaptive.
- Visual stimuli were improved and simplified to produce more robust visual responses.
- The complete kit was tested on 25 normal observers naive to the purpose of the test and two observers with possible visual dysfunctions resulting from recent TBI and retinal detachment injuries.
- When compared with normal subjects the two observers with possible visual dysfunctions showed significantly lower scores which appear to be in agreement with their prior symptoms and clinical histories.

Reportable Outcomes

There were no reportable outcomes yet.

Conclusions

We significantly improved the battery of tests designed to diagnose various visual dysfunctions. All hardware and software components of data acquisition and analysis pipeline are in place now allowing data collection and analysis in real-time regime. The visual stimulation and data collection units were tested on 25 naive observers with normal vision and 2 observers with possible visual dysfunctions. We used the collected data to make a pilot comparison of oculomotor responses between normal subjects and subjects with visual dysfunctions. The results indicated that the adopted paradigm could successfully diagnose visual dysfunctions. This mostly completes the second phase of the project and allows us to start the last phase, which mainly focuses on the two goals: testing a large number of normal subjects to establish the distribution of responses for people with normal (reference) visual functions, and testing subjects with visual/cognitive dysfunctions to validate the proposed approach.